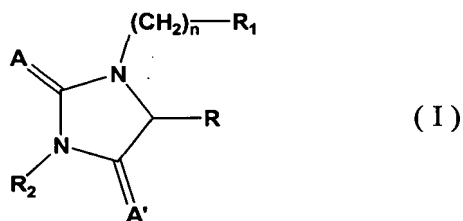


WHAT IS CLAIMED IS:

1. A compound having the Formula I:



or a pharmaceutically acceptable salt, or solvate thereof, wherein:

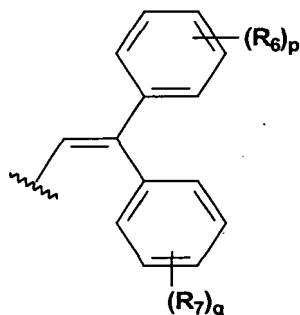
$n$  is 0 to 3;

$\text{A}$  and  $\text{A}'$  are independently oxygen or sulfur;

$\text{R}$  is hydrogen, linear or branched alkyl, benzyl, hydroxybenzyl, thioalkyl, alkylthioalkyl, hydroxyalkyl, aminoalkyl, guanidinylalkyl, carboxyalkyl or aminocarboxyalkyl;

$\text{R}_1$  is selected from the group consisting of:

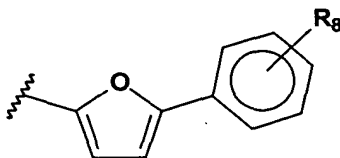
- (i) optionally substituted phenoxyphenyl;
- (ii) optionally substituted benzyloxyphenyl;
- (iii) optionally substituted phenylthiophenyl;
- (iv) optionally substituted benzylthiophenyl;
- (v) optionally substituted phenylaminophenyl;
- (vi) optionally substituted benzylaminophenyl; and
- (vii)



wherein each occurrence of  $\text{R}_6$  and each occurrence of  $\text{R}_7$  are independently hydrogen or alkyl; and

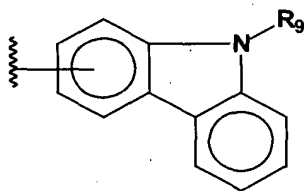
$p$  and  $q$  are independently integers from zero to 4;

(viii)



wherein R<sub>8</sub> is hydrogen, halogen, hydroxy, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, cyano, amino, or nitro;

(ix)



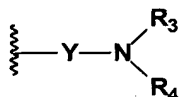
wherein R<sub>9</sub> is hydrogen or C<sub>1-6</sub> alkyl; and

(x) optionally substituted naphthdyl;

and

R<sub>2</sub> is selected from the group consisting of:

(i)



where

Y is an optionally substituted C<sub>2-6</sub> alkylene, and

R<sub>3</sub> and R<sub>4</sub> are the same or different and are hydrogen, alkyl, or aryl, or R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain having 3 to 5 carbon atoms, optionally substituted with an alkyl or aryl moiety, or said alkylene chain is optionally interrupted by an oxygen atom or -NR<sub>5</sub>, where R<sub>5</sub> is hydrogen or C<sub>1-6</sub> alkyl;

(ii) pyridylalkyl; and

(iii) piperidin-4-ylalkyl, optionally substituted by alkyl, aryl or aralkyl.

2. The compound according to claim 1, wherein R<sub>2</sub> is -YNR<sub>3</sub>R<sub>4</sub>, and an optionally substituted C<sub>2-6</sub> alkylene.

3. The compound according to claim 2, wherein:

R<sub>1</sub> is optionally substituted phenoxyphenyl or optionally substituted benzyloxyphenyl; R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain having 4 to 5 carbon atoms; and Y is an optionally substituted C<sub>2-4</sub> alkylene chain.

4. The compound according to claim 3, wherein R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain of 5 carbon atoms; and Y is an optionally substituted C<sub>2-4</sub> alkylene chain.

5. The compound according to claim 3, wherein R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain of 4 carbon atoms, and Y is an optionally substituted C<sub>2-4</sub> alkylene chain.

6. The compound according to claim 2, wherein Y is ethylene or propylene.

7. The compound according to claim 2, wherein:

R<sub>1</sub> is optionally substituted phenoxyphenyl or optionally substituted benzyloxyphenyl; R<sub>3</sub> and R<sub>4</sub> are independently hydrogen, alkyl or aryl; and Y is an optionally substituted C<sub>2-4</sub> alkylene chain.

8. The compound according to claim 1, wherein n is 1.

9. The compound according to claim 1, wherein n is 0.

10. The compound according to claim 1, wherein R<sub>1</sub> is an optionally substituted phenoxyphenyl.

11. The compound according to claim 1, wherein R<sub>1</sub> is an optionally substituted benzyloxyphenyl.

12. The compound according to claim 1, wherein  $-(CH_2)_n-$  is attached to the 3- or 4-position of the phenyl component of the phenoxyphenyl or the benzyloxyphenyl defined by  $R_1$ .

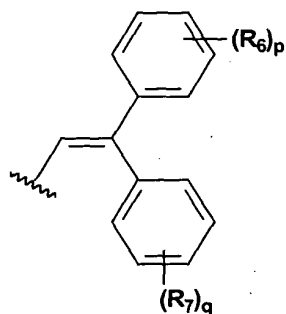
13. The compound according to claim 10, wherein  $n$  is 1;  $R_2$  is  $-YNR_3R_4$ ,  $Y$  is  $C_{2-6}$  alkylene; and  $R_3$  and  $R_4$  together form an alkylene chain having 4 to 5 carbon atoms.

14. The compound according to claim 11, wherein  $n$  is 1;  $R_2$  is  $-YNR_3R_4$ ,  $Y$  is  $C_{2-6}$  alkylene; and  $R_3$  and  $R_4$  together form an alkylene chain having 4 to 5 carbon atoms.

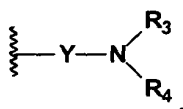
15. The compound according to claim 10, wherein  $n$  is 1;  $R_2$  is  $-YNR_3R_4$ ,  $Y$  is  $C_{2-6}$  alkylene; and  $R_3$  and  $R_4$  are the same or different and are selected from hydrogen, alkyl, or aryl.

16. The compound according to claim 11, wherein  $n$  is 1;  $R_2$  is  $-YNR_3R_4$ ,  $Y$  is  $C_{2-6}$  alkylene; and  $R_3$  and  $R_4$  are the same or different and are selected from hydrogen, alkyl, or aryl.

17. The compound according to claim 1, wherein  $R_1$  is



18. The compound according to claim 17, wherein  $R_2$  is

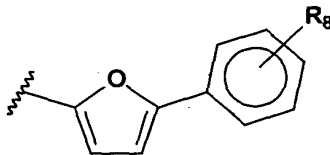


19. The compound according to claim 17 wherein Y is a C<sub>2-6</sub> alkylene, and R<sub>3</sub> and R<sub>4</sub> are the same or different and are selected from hydrogen, alkyl, or aryl.

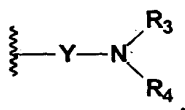
20. The compound according to claim 18, wherein Y is a C<sub>2-6</sub> alkylene, and, R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.

21. The compound according to claim 20, wherein said alkylene chain formed from taking R<sub>3</sub> and R<sub>4</sub> together is further interrupted by an oxygen atom or -NR<sub>5</sub>, where R<sub>5</sub> is hydrogen or C<sub>1-6</sub> alkyl.

22. The compound according to claim 1, wherein R<sub>1</sub> is



23. The compound according to claim 22, wherein R<sub>2</sub> is

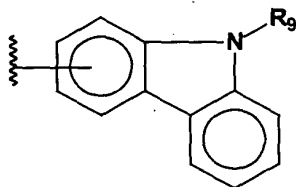


24. The compound according to claim 23, wherein Y is a C<sub>2-6</sub> alkylene, and R<sub>3</sub> and R<sub>4</sub> are the same or different and are selected from hydrogen, alkyl, or aryl.

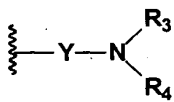
25. The compound according to claim 23, wherein Y is a C<sub>2-6</sub> alkylene, and, R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.

26. The compound according to claim 25, wherein said alkylene chain formed from taking R<sub>3</sub> and R<sub>4</sub> together is further interrupted by an oxygen atom or -NR<sub>5</sub>, where R<sub>5</sub> is hydrogen or alkyl.

27. The compound according to claim 1, wherein  $R_1$  is



28. The compound according to claim 27, wherein  $R_2$  is



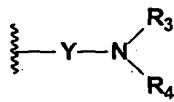
29. The compound according to claim 28, wherein Y is a  $C_{2-6}$  alkylene, and  $R_3$  and  $R_4$  are the same or different and are selected from hydrogen, alkyl, or aryl.

30. The compound according to claim 28, wherein Y is a  $C_{2-6}$  alkylene, and,  $R_3$  and  $R_4$  together form an alkylene chain having 4 to 5 carbon atoms, optionally substituted with an alkyl or aryl moiety.

31. The compound according to claim 30, wherein said alkylene chain formed from taking  $R_3$  and  $R_4$  together is further interrupted by an oxygen atom or  $-NR_5$ , where  $R_5$  is hydrogen or alkyl.

32. The compound according to claim 1, wherein  $R_1$  is naphthyl.

33. The compound according to claim 31, wherein  $R_2$  is



34. The compound according to claim 32, wherein Y is a C<sub>2-6</sub> alkylene, and R<sub>3</sub> and R<sub>4</sub> are the same or different and are selected from hydrogen, alkyl, or aryl.
35. The compound according to claim 33, wherein Y is a C<sub>2-6</sub> alkylene, and, R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.
36. The compound according to claim 35, wherein said alkylene chain is further interrupted by an oxygen atom or -NR<sub>5</sub>, where R<sub>5</sub> is hydrogen or alkyl.
37. The compound according to claim 1, wherein said compound is selected from the group consisting of:
- 3-(2-piperidinyethyl)-1-(4-(4-fluorophenoxy)benzyl) hydantoin;
  - 3-(2-piperidinyethyl)-1-(4-(benzyloxy)benzyl) hydantoin;
  - 3-(2-piperidinyethyl)-1-(3-(4-trifluoromethylphenoxy)benzyl) hydantoin;
  - 3-(2-piperidinyethyl)-1-(3-(3,4-dichlorophenoxy)benzyl) hydantoin;
  - 3-(2-piperidinyethyl)-1-(3-(phenoxy)benzyl) hydantoin; and
  - 3-(2-piperidinyethyl)-1-(3-(benzyloxy)benzyl) hydantoin.
38. A pharmaceutical composition, comprising the compound of claim 1, and a pharmaceutically acceptable carrier or diluent.
39. A method of making a compound according to claim 1 wherein said method comprises:
- (a) reacting an amine-protected amino acid with a resin-supported hydroxy group to produce a resin-supported, amine-protected, amino acid;
  - (b) deprotecting said resin-supported amine-protected amino acid, to produce a resin-supported amino acid having an N-terminus primary amine;
  - (c) reacting said resin-supported amino acid obtained in step (b), with an aldehyde to produce a resin-supported enamine;

(d) reducing said resin-supported enamine obtained in from step (c), to produce a resin-supported amino acid, having an N-terminus secondary amine;

(e) reacting said resin-supported amino acid obtained from step (d), with triphosgene, to produce a resin-supported amino acid having an N-terminus tertiary amine, wherein said tertiary amine comprises a carbonyl chloride moiety;

(f) reacting said resin-supported amino acid obtained from step (e), with a primary amine; and

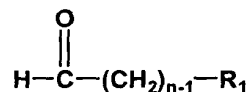
(g) releasing a product obtained from step (f) from its support, to obtain the compound of Formula I.

40. The method according to claim 39, wherein said resin is a Wang resin.

41. The method according to claim 39, wherein step (a) is carried out in the presence of DMF, DIC and DMAP.

42. The method according to claim 39, wherein step (b) is carried out in the presence of piperidine and DMF.

43. The method according to claim 39, wherein said aldehyde of step (c) has the formula:



wherein:

n is an integer from 1-3; and

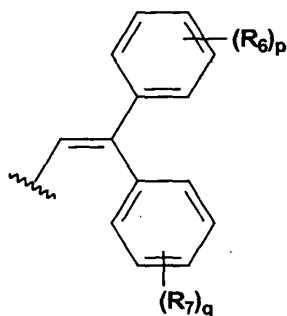
R<sub>1</sub> is selected from the group consisting of:

- (i) optionally substituted phenoxyphenyl;
- (ii) optionally substituted benzyloxyphenyl;
- (iii) optionally substituted phenylthiophenyl;
- (iv) optionally substituted benzylthiophenyl;
- (v) optionally substituted phenylaminophenyl;



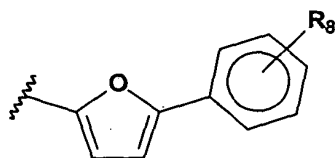
(vi) optionally substituted benzylaminophenyl;

(vii)



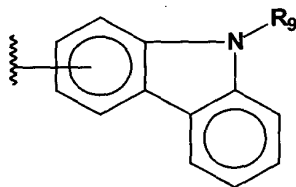
wherein  $R_6$  and  $R_7$  are independently hydrogen or alkyl; and  $p$  and  $q$  are independently integers from 0 to 4;

(viii)



wherein  $R_8$  is hydrogen or alkyl;

(ix)

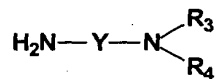


wherein  $R_9$  is hydrogen or alkyl; and

(x) naphthyl.

44. The method according to claim 39, wherein said primary amine of step (f) is selected from the group consisting of:

(i) an amine of the formula:



wherein

$Y$  is an optionally substituted  $C_{2-6}$  alkylene; and

R<sub>3</sub> and R<sub>4</sub> are the same or different and are selected from hydrogen, alkyl, or aryl, or R<sub>3</sub> and R<sub>4</sub> together form an alkylene chain having 4 to 5 carbon atoms, optionally substituted with an alkyl or aryl moiety, and said alkylene chain is optionally interrupted by an oxygen atom or -NR<sub>5</sub>, where R<sub>5</sub> is hydrogen or alkyl;

- (ii) pyridylalkyl amine; and
- (iii) an optionally substituted piperidin-4-ylalkyl amine, wherein optional substituents are selected from the group consisting of alkyl, aryl or aralkyl.

45. The method according to claim 44, wherein said primary amine is 1-(2-aminoethyl)piperidine; (2-aminoethyl)pyrrolidine; or di(2-propyl)(2-aminoethyl) amine.

46. The method according to claim 39, wherein step (e) is carried out in the presence of DMF and pyridine.

47. A method of treating, preventing or ameliorating a disorder responsive to blockage of sodium channels in a mammal, comprising administering to a mammal in need thereof an effective amount of a compound according to claim 1, or pharmaceutically acceptable salt thereof.

48. The method according to claim 47, wherein said disorder is selected from the group consisting of: neuronal damage; a neurodegenerative condition, acute or chronic pain, depression, and diabetic neuropathy.

49. The method according to claim 47, wherein said neuronal damage is caused by focal or global ischemia.

50. The method according to claim 47, wherein said neurodegenerative condition is amyotrophic lateral sclerosis (ALS).

51. The compound according to claim 1, wherein said compound functions as an antitinnitus agent, anticonvulsant, antiarrhythmic, local anesthetic, or antimanic depressant.

52. A method of treating a mammal suffering from a disorder responsive to blockage of sodium channels, said method comprising administering to said mammal a compound according to claim 1, or pharmaceutically acceptable salt thereof, in an amount that is effective for treating said disorder.

53. The method according to claim 52 wherein said mammal is a human, dog or cat.

54. The method according to claim 53, wherein said disorder is selected from the group consisting of: neuronal damage; a neurodegenerative condition, acute or chronic pain, depression, and diabetic neuropathy.

55. The method according to claim 53, wherein said neuronal damage is caused by focal or global ischemia.

56. The method according to claim 53, wherein said neurodegenerative condition is amyotrophic lateral sclerosis (ALS).

57. The compound according to claim 37, wherein the compound is selected from the group consisting of:

3-(2-piperidinyloethyl)-1-(3-(4-trifluoromethylphenoxy)benzyl)

hydantoin;

3-(2-piperidinyloethyl)-1-(3-(3,4-dichlorophenoxy)benzyl)hydantoin;

and

3-(2-piperidinyloethyl)-1-(3-(benzyloxy)benzyl)hydantoin.